

**Table 1. Participation of Case and Control Subjects, Atlanta, Georgia, 1989 - 1996**

<b>Disposition</b>	<b>DS Cases</b>			<b>Controls</b>
	<b>Liveborn<sup>%</sup></b>	<b>Pregnancy terminations</b>	<b>Total</b>	
Participated	249	36	285	329
Refused	47	33	80	77
Proband died	19	-	19	0
Proband adopted	7	-	7	0
Lost to follow-up	9	40	49	61
In progress <sup>†</sup>	27	5	32	57
Total in 5-county area	358	114 <sup>‡</sup>	472	524
Participation rate	70%	32%	60%	63%

<sup>%</sup> Seven mosaic DS cases were excluded from this total.

<sup>†</sup> Includes cases and controls currently being tracked as well as cases in which genotyping studies are in progress.

<sup>‡</sup> This number represents only a portion of total pregnancies terminated for trisomy 21 in the 5-county area. The total number is unknown.

**Table 2. Parent of Origin and Timing of the Nondisjunctional Error in Nonmosaic DS.**

	Liveborn	TAB <sup>%</sup>	Total	Proportion
<b>Paternal:</b>				
Meiosis I (PMI)	10	1	11	PMI/(PMI+PMII)= 11/19= 57.9%
Meiosis II (PMII)	7	1	8	PMII/(PMI+PMII)= 8/19=42.1%
Stage unknown	1	1	2	
Subtotal	18	3	21	<b>Pat/All meiotics= 21/237 = 8.9%</b>
<b>Maternal:</b>				
Meiosis I (MMI)	151	18	169	MMI/(MMI+"MMII")=169/206=82.0%
"Meiosis II" ("MMII")	35	2	37	"MMII"/(MMI+"MMII")=37/206=18.0%
Stage unknown	9	1	10	
Subtotal	195	21	216	<b>Mat/All meiotics = 216/237= 91.1%</b>
<b>Mitotics</b>	11	1	12	Mitotics/All known =12/249=4.8%
<b>Unknown</b>	25	11	36	Unknown/All= 36/285=12.6%
<b>Total cases</b>	249	36	285	

<sup>%</sup> TAB = therapeutic abortion.

MMI & "MMII" indicate origin and timing of nondisjunction (see text).

**Table 3. Selected Characteristics of Case and Control Mothers by Parent of Origin and Timing of Nondisjunction of Chromosome 21.**

Characteristic	All Meiotic Cases‡		All Maternal		MMI		"MMII"		Controls	
	N		N		N		N		N	
Mean maternal age (SD)	273	31.5 (6.9)	216	31.7 (6.8)	169	31.8 (6.6)	37	32.4 (7.4)	329	27.5 (6.2)
Mean parity (SD)	273	2.1 (1.4)	216	2.1 (1.4)	169	2.0 (1.2)	37	2.5 (2.0)	329	2.0 (1.3)
Mean N of miscarriages (SD)	273	0.38 (0.7)	216	0.32 (0.7)	169	0.33 (0.7)	37	0.30 (0.7)	329	0.33 (0.7)
<b>Education</b>										
Less than high school	35	12.8%	24	11.1%	19	11.2%	4	10.8%	63	19.2%
High school+	238	87.2%	192	88.9%	150	88.8%	33	89.2%	266	80.8%
<b>Race</b>										
White	162	59.3%	130	60.2%	100	59.2%	24	64.9%	162	49.2%
Black	89	32.6%	69	31.9%	56	33.1%	10	27.0%	142	43.2%
Other	22	8.1%	17	7.9%	13	7.7%	3	8.1%	25	7.6%
<b>Maternal smoking</b>										
Never smoked	187	68.5%	152	70.4%	120	71.0%	24	64.9%	225	71.0%
Ever smoked	86	31.5%	64	29.6%	49	29.0%	13	35.1%	95	28.9%
Current smoker*	42	15.4%	29	13.4%	20	11.8%	8	21.6%	52	15.8%
Total pack-years < 5	44	16.1%	32	14.8%	26	15.4%	6	16.2%	54	16.4%
\$ 5	42	15.4%	32	14.8%	23	13.6%	7	18.9%	40	12.2%
<b>Maternal OC use</b>										
Never used OC	48	17.6%	39	18.1%	25	17.1%	6	14.3%	56	17.0%
Prior OC users	225	82.4%	177	81.9%	121	82.9%	36	85.7%	273	83.0%
Current OC user†	24	8.8%	18	8.3%	12	8.2%	5	11.9%	49	15.0%

MMI & "MMII" indicate origin and timing of nondisjunction (see text).

\* Current smoker includes mothers who smoked any time from 2 months before to 2 months after conception of the index case.

† Current OC user includes mothers who used OC any time from 2 months before to 2 months after conception of the index case. All "current OC users", except one case mother, also had a history of prior OC use sometime during their reproductive years.

‡ The category "All Meiotic Cases" includes the cases of unknown origin. A small proportion of these unknown cases may be mitotic in origin.

**Table 4. Association of Maternal Smoking with Nondisjunction of Chromosome 21 by Origin of Error and Maternal Age: Adjusted Odds Ratio (OR) and 95% Confidence Intervals (CI)**

Characteristic	All Ages			<35 Years			\$35 Years		
	Case	Control	OR (95% CI)	Case	Control	OR (95% CI)	Case	Control	OR (95% CI)
<b>All meiotic cases‡</b>	273	329		175	292		98	37	
Never smoked	187	234	1.0	122	212	1.0	65	22	1.0
Ever smoked	86	95	0.96 (0.66-1.40)	53	80	1.04 (0.67-1.60)	33	15	0.89 (0.39-2.03)
Current smoker%	42	52	0.96 (0.60-1.54)	30	47	1.03 (0.61-1.73)	12	5	1.15 (0.31-4.22)
Total pack-years									
< 5	44	54 <sup>†</sup>	1.01 (0.64-1.61)	32	47	1.13 (0.68-1.89)	12	7	0.60 (0.21-1.76)
\$ 5	42	40	0.94 (0.57-1.56)	21	32	0.95 (0.51-1.77)	21	8	1.24 (0.43-3.54)
<b>All maternal cases</b>	216	329		137	292		79	37	
Never smoked	152	234	1.0	96	212	1.0	56	22	1.0
Ever smoked	64	95	0.89 (0.60-1.33)	41	80	0.98 (0.62-1.57)	23	15	0.71 (0.30-1.67)
Current smoker%	29	52	0.84 (0.50-1.42)	21	47	0.90 (0.50-1.62)	8	5	0.82 (0.20-3.30)
Total pack-years									
< 5	32	54 <sup>†</sup>	0.91 (0.55-1.51)	24	47	1.06 (0.60-1.85)	8	7	0.44 (0.14-1.40)
\$ 5	32	40	0.90 (0.53-1.55)	17	32	0.93 (0.48-1.80)	15	8	1.03 (0.35-3.09)

(continued)

**Table 4. Continued**

<b>MMI cases</b>	169	329		107	292		62	37	
Never smoked	120	234	1.0	78	212	1.0	42	22	1.0
Ever smoked	49	95	0.85 (0.55-1.32)	29	80	0.86 (0.51-1.44)	20	15	0.78 (0.32-1.89)
Current smoker <sup>*</sup>	20	52	0.72 (0.40-1.29)	13	47	0.69 (0.35-1.37)	7	5	0.81 (0.20-3.29)
Total pack-years									
< 5	26	54 <sup>†</sup>	0.92 (0.54-1.59)	19	47	1.03 (0.56-1.89)	7	7	0.47 (0.14-1.60)
\$ 5	23	40	0.80 (0.44-1.45)	10	32	0.67 (0.31-1.47)	13	8	1.13 (0.37-3.40)
<b>"MMII" cases</b>	37	329		21	292		16	37	
Never smoked	24	234	1.0	11	212	1.0	13	22	1.0
Ever smoked	13	95	1.14 (0.54-2.40)	10	80	2.43 (0.89-6.63)	3	15	0.37 (0.07-1.87)
Current smoker <sup>*</sup>	8	52	1.55 (0.64-3.76)	7	47	2.98 (1.01-8.87)	1	5	0.65 (0.06-7.48)
Total pack-years									
< 5	6	54 <sup>†</sup>	1.04 (0.39-2.75)	5	47	2.23 (0.68-7.32)	1	7	0.24 (0.02-2.56)
\$ 5	7	40	1.28 (0.49-3.30)	5	32	2.80 (0.82-9.59)	2	8	0.50 (0.08-3.33)

MMI & "MMII" indicate origin and timing of nondisjunction (see text). Odds ratios were adjusted for maternal age (as a continuous variable), educational attainment, and racial group.

<sup>\*</sup> Current smoker includes mothers who smoked any time between 2 months before and 2 months after conception of the index case.

<sup>†</sup> One control was excluded in calculating total pack-years of smoking because information on number of cigarettes smoked was not available.

<sup>‡</sup> The category "All Meiotic Cases" includes the cases of unknown origin. A small proportion of these unknown cases may be mitotic in origin.

**Table 5. Association of Maternal Smoking and Oral Contraceptive Use around the Time of Conception with Nondisjunction of Chromosome 21 (by Origin of the Error and Maternal Age). Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI)**

All Ages					< 35 Years			\$ 35 Years		
Smoking	OC use	Case	Contro l	OR (95% CI)	Case	Contro l	OR (95% CI)	Case	Control	OR (95% CI)
All Maternal										
-	-	174	235	1.0	105	203	1.0	69	32	1.0
-	+	13	42	0.59 (0.30-1.16)	11	42	0.55 (0.27-1.13)	2	0	-
+	-	24	45	0.73 (0.42-1.28)	16	40	0.73 (0.38-1.38)	8	5	0.95 (0.24-3.74)
+	+	5	7	1.36 (0.40-4.61)	5	7	1.41 (0.43-4.36)	0	0	-
MMI										
-	-	139	235	1.0	85	203	1.0	54	32	1.0
-	+	10	42	0.58 (0.27-1.21)	9	42	0.56 (0.26-1.21)	1	0	-
+	-	18	45	0.67 (0.37-1.25)	11	40	0.62 (0.30-1.27)	7	5	0.89 (0.23-3.54)
+	+	2	7	0.70 (0.14-3.61)	2	7	0.76 (0.15-3.76)	0	0	-
"MMII"										
-	-	27	235	1.0	13	203	1.0	14	32	1.0
-	+	2	42	0.66 (0.15-3.00)	1	42	0.38 (0.05-3.01)	1	0	-
+	-	5	45	1.06 (0.38-3.01)	4	40	1.54 (0.45-5.27)	1	5	1.03 (0.09-11.7)
+	+	3	7	5.82 (1.28-26.4)	3	7	7.62 (1.63-35.6)	0	0	-

MMI & "MMII" indicate origin and timing of nondisjunction (see text). Odds ratios were adjusted for maternal age (as a continuous variable), educational attainment, and racial group. Smoking and oral contraceptive use are two dichotomous variables: current smokers (smoking at ±2 months of conception of index case) vs non smokers (see text for explanation), and OC user (±2 months of conception of index case) vs not OC users. Plus sign (+) indicates exposure, and minus sign (-) indicates no exposure.

**Table 6. Association of Maternal Smoking and OC Use with "MMII" Nondisjunction of Chromosome 21 Using Affected Controls. Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI).**

"MMII"		All Ages			< 35 Years			\$ 35 Years		
Maternal smoking		Cas e	Affected control <sup>%</sup>	OR (95% CI) <sup>†</sup>	Case	Affected control <sup>%</sup>	OR (95% CI) <sup>†</sup>	Case	Affected control <sup>%</sup>	OR (95% CI) <sup>†</sup>
Never smoked		24	169	1.0	11	115	1.0	13	54	1.0
Ever-smoked		13	79	1.12 (0.53-2.36)	10	47	2.33 (0.86-6.29)	3	32	0.28 (0.06-1.31)
Current smoker		8	38	1.52 (0.62-3.76)	7	26	3.20 (1.05-9.76)	1	12	-‡
Total pack-years										
< 5		6	41	1.04 (0.39-2.72)	5	29	1.82 (0.56-5.94)	1	12	0.35 (0.04-3.03)
\$ 5		7	38	1.21 (0.54-3.18)	5	18	3.37 (0.94-12.1)	2	20	0.23 (0.03-1.86)
Maternal smoking and OC use										
Smoking	OC use									
-	-	27	193	1.0	13	120	1.0	14	73	1.0
-	+	2	17	1.04 (0.21-5.02)	1	16	0.45 (0.05-3.97)	1	1	6.90 (0.32-146.8)
+	-	5	34	1.09 (0.38-3.12)	4	22	1.96 (0.55-6.93)	1	12	-‡
+	+	3	4	6.18 (1.24-30.8)	3	4	6.86 (1.32-35.7)	0	0	-

MMI & "MMII" indicate origin and timing of nondisjunction (see text). Odd ratios were adjusted for maternal age, educational attainment and race.

Smoking and oral contraceptive use are two dichotomous variables: current smokers (smoking at  $\pm 2$  months of conception of index case) vs non smokers (see text for explanation), and OC use at  $\pm 2$  months of conception of index case vs not OC users. Plus sign (+) indicates exposure, and minus sign (-) indicates non-exposure.

<sup>%</sup> Affected controls includes all Down syndrome cases except MMII cases (including 12 cases of mitotic origin).

<sup>†</sup> Odds ratios were adjusted for maternal age (as a continuous variable), educational attainment, and racial group.

<sup>‡</sup> The estimates of odds ratios were unstable due to the small numbers.